

## REMARKS

The amendments to the claims are designed to place the application in a position for allowance. While applicants do not concede that Bowles in any way fairly suggests the subject matter of the claims prior to amendment, in order to expedite prosecution, the limitations of claim 3 has been amended into claim 1. Claim 3 was not rejected over the art. Claims 12, 56, 58, 125, 129 and 131 have been amended to accommodate the criticism of the term "comprises" or "comprising." In addition, claims 12, 56, 125 and 129 have been amended to delete "selected from the group consisting of:" as it is not needed in view of the words that follow that phrase. Claim 98 has been amended to place it in independent form in the event that any of the compounds listed are outside the scope of claim 1 as amended. Claim 119 has also been amended to place it in independent form as the limitations of claim 3 are not needed; it will be noted that the claim is identical in scope to that previously proposed. Clearly no new matter has been added and entry of the amendment is respectfully requested.

### The Rejections

With regard to claim 1, and, now, claim 119 which has been converted to independent form, the suggestions kindly made by the Examiner have been adopted. "And" before "the pharmaceutically acceptable acid addition salts thereof" has been changed to "or" and the reference to stereoisomers has been corrected.

With respect to the rejection of claims 12, 56, 58, 125, 129 and 131, applicants have amended the claims to substitute "contains" or "containing" for "comprising." Applicants note that the Examiner considers "containing" synonymous with "comprising"; however, "containing" does not have the legal baggage as a term of art. It is believed that the claims are now clear; for example, in claim 12, the ring must in fact have 1-4 heteroatoms in it. It is believed there is no implication that the requirement that the ring contain 1-4 heteroatoms somehow admits further incorporations into the ring.

Claims 58 and 131 have also been reworded to change "may optionally be" to "are optionally," which applicants believe is more definitive.

In light of the foregoing amendments, it is believed that the rejection under 35 U.S.C. § 112, second paragraph, can be withdrawn.

With respect to the rejection over Bowles, claim 1 has been amended to incorporate the limitations of claim 3 and claim 3 is therefore canceled. Claim 3 was not rejected over Bowles and so, with these additional limitations, it is clear that claim 1 as amended is free of Bowles as well. Claims 7 and 102, which were included in the rejection over Bowles but dependent on claim 1, are therefore free of this art as well.

It is believed that the rejection of claims 119-120 and 132 over Bowles is in error. Claim 119 has been placed into independent form as the limitations added to claim 1 are not necessary for this claim. It will be noted that there is no Bowles compound that contains two nitrogens, neither of which is included in a ring, where the two N are separated by an intervening aryl group as required by the present compounds. The only embodiments of Bowles which contain two nitrogens, neither of which is included in a ring, are those wherein B represents a  $\text{CH}_2\text{NR}^9\text{NR}^{10}$  group or a  $\text{CONR}^9\text{R}^{10}$  group. In these instances, there is no aryl group forming a link in the chain between the two nitrogens as required by the present claims. Accordingly, these compounds are not included in the genus described by Bowles. Accordingly, it is believed that claims 119-132 are clearly in a position for allowance.

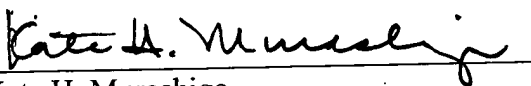
In view of the foregoing amendment and discussion, passage of claims 1-2, 4, 6-7, 12-13, 51, 55-58, 98, 102, and 119-132 to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket No. 391442003700.

Dated: December 30, 2002

By:

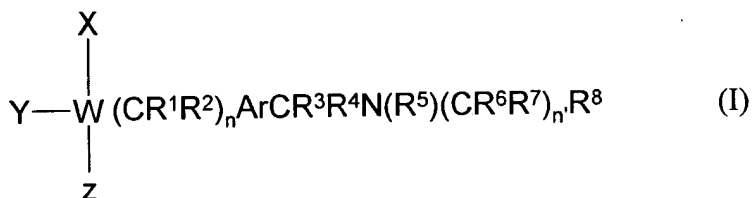
Respectfully submitted,

  
Kate H. Murashige  
Registration No. 29,959  
Morrison & Foerster LLP  
3811 Valley Centre Drive, Suite 500  
San Diego, California 92130-2332  
Telephone: (858) 720-5112  
Facsimile: (858) 720-5125

# EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

## In the Claims:

1. (Five times amended) A compound according to Formula I:



wherein, W is a nitrogen atom and Y is void or, W is a carbon atom and Y=H;

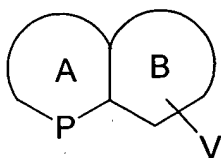
R<sup>1</sup> to R<sup>7</sup> may be the same or different and are independently hydrogen or straight, branched or cyclic C<sub>1-6</sub> alkyl;

R<sup>8</sup> is an optionally substituted heterocyclic group or an optionally substituted aromatic group

Ar is an aromatic or heteroaromatic ring optionally substituted at single or multiple, non-linking positions with electron-donating or withdrawing groups;

n and n' are independently, 0-2;

X is a group of the formula:



wherein, Ring A is an optionally substituted, saturated or unsaturated 5 or 6-membered ring, and P is an optionally substituted nitrogen atom and wherein any heteroatom in ring A or B is N;

wherein Ring B is an optionally substituted 5 to 7-membered ring;

wherein Ring A or Ring B is bound to group W from any position through group V;

wherein V is a chemical bond or V is a (CH<sub>2</sub>)<sub>n''</sub> group (where n''= 1-2), or V is a C=O group; and

wherein Z is selected from the group consisting of: a hydrogen atom; an optionally substituted C<sub>1-6</sub> alkyl group; an optionally substituted aromatic or heterocyclic group; a C<sub>1-6</sub> alkyl group substituted with an optionally substituted aromatic or heterocyclic group; an optionally

substituted amino group; an optionally substituted C<sub>1-6</sub> alkylamino or C<sub>3-7</sub> cycloalkylamino group; a sulfonyl group and an optionally substituted carbonyl group; [and] or the pharmaceutically acceptable acid addition salts thereof; [and] including said compound in any stereoisomeric [forms and mixtures] form and mixture of stereoisomeric forms thereof; wherein Ring B is selected from the group consisting of: benzene and a 5 to 7-membered cycloalkyl ring; and the optionally substituted forms thereof.

12. (Twice amended) The compound of claim 1 wherein said optional substituent in Ring A or Ring B is independently an optionally substituted aralkyl or heterocycloalkyl, wherein said heterocycloalkyl [comprises] is a 5 or 6 membered ring [comprising] containing 1-4 heteroatoms.

56. (Amended) The compound of claim 55, wherein said optionally substituted aromatic group is substituted with a substituent selected from the group consisting of: benzene; naphthalene; dihydronaphthalene; and tetrahydronaphthalene; and wherein said optionally substituted heterocyclic group is [selected from the group consisting of:] a 5 to 6-membered saturated, partially saturated, or aromatic heterocyclic ring [comprising] containing 1 to 4 heteroatoms selected from nitrogen, oxygen and sulfur.

58. (Twice amended) The compound of claim 57, wherein said heterocyclic group [comprises] contains nitrogen or sulfur heteroatoms; and wherein said nitrogen or sulfur heteroatoms [may] are optionally [be] in the form of oxides.

98. (Twice amended) A compound [of claim 1] selected from the group consisting of:

- (aaa) AMD8862, N-(2-pyridinylmethyl)-N'-[2-[(1*H*-imidazol-4-ylmethyl)amino]ethyl]-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzene dimethanamine;
- (bbb) AMD8887, N-(2-pyridinylmethyl)-N'-[2-[(1*H*-imidazol-2-ylmethyl)amino]ethyl]-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;

- (ccc) AMD8816, N-(2-pyridinylmethyl)-N'-[2-(phenylureido)ethyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (ddd) AMD8737, N-(2-pyridinylmethyl)-N'-[[N''-(n-butyl)carboxamido]methyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (eee) AMD8739, N-(2-pyridinylmethyl)-N'-(carboxamidomethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (fff) AMD8752, N-(2-pyridinylmethyl)-N'-[(N''-phenyl)carboxamidomethyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (ggg) AMD8765, N-(2-pyridinylmethyl)-N'-(carboxymethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (hhh) AMD8715, N-(2-pyridinylmethyl)-N'-(phenylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (iii) AMD8907, N-(2-pyridinylmethyl)-N'-(1*H*-benzimidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (jjj) AMD8927, N-(2-pyridinylmethyl)-N'-(5,6-dimethyl-1*H*-benzimidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine (hydrobromide salt);
- (kkk) AMD8926, N-(2-pyridinylmethyl)-N'-(5-nitro-1*H*-benzimidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (lll) AMD8929, N-(2-pyridinylmethyl)-N'-[(1*H*)-5-azabenzimidazol-2-ylmethyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (mmm) AMD8931, N-(2-pyridinylmethyl)-N-(4-phenyl-1*H*-imidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (nnn) AMD8783, N-(2-pyridinylmethyl)-N'-[2-(2-pyridinyl)ethyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (ooo) AMD8764, N-(2-pyridinylmethyl)-N'-(2-benzoxazolyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (ppp) AMD8780, N-(2-pyridinylmethyl)-N'-(*trans*-2-aminocyclohexyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (qqq) AMD8818, N-(2-pyridinylmethyl)-N'-(2-phenylethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (rrr) AMD8829, N-(2-pyridinylmethyl)-N'-(3-phenylpropyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;

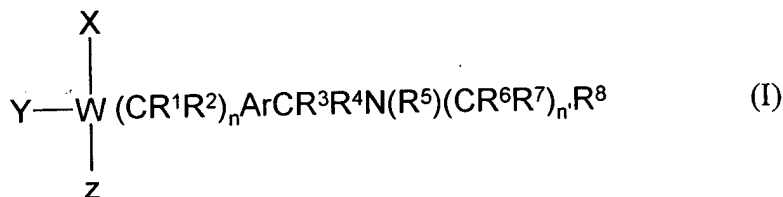
- (sss) AMD8839, N-(2-pyridinylmethyl)-N'-(*trans*-2-aminocyclopentyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (ttt) AMD8726, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-glycinamide;
- (uuu) AMD8738, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-(L)-alaninamide;
- (vvv) AMD8749, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-(L)-aspartamide;
- (www) AMD8750, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-pyrazinamide;
- (xxx) AMD8740, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-(L)-prolinamide;
- (yyy) AMD8741, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-(L)-lysineamide;
- (zzz) AMD8724, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-benzamide;
- (aaaa) AMD8725, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-picolinamide;
- (bbbb) AMD8713, N'-Benzyl-N-[[4-[(2-pyridinylmethyl) amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-urea;
- (cccc) AMD8712, N'-phenyl-N-[[4-[(2-pyridinylmethyl) amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinoliny)-urea;
- (dddd) AMD8716, N-(6,7,8,9-tetrahydro-5*H*-cyclohepta[*bacteriapyridin*-9-yl)-4-[(2-pyridinylmethyl)amino]methyl]benzamide;
- (eeee) AMD8717, N-(5,6,7,8-tetrahydro-8-quinoliny)-4-[(2-pyridinylmethyl)amino]methyl]benzamide;
- (ffff) AMD8634, N,N'-bis(2-pyridinylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (gggg) AMD8774, N,N'-bis(2-pyridinylmethyl)-N'-(6,7,8,9-tetrahydro-5*H*-cyclohepta[*bacteriapyridin*-9-yl)-1,4-benzenedimethanamine;
- (hhhh) AMD8775, N,N'-bis(2-pyridinylmethyl)-N'-(6,7-dihydro-5*H*-cyclopenta[*bacteriapyridin*-7-yl)-1,4-benzenedimethanamine;

- (iiii) AMD8819, N,N'-bis(2-pyridinylmethyl)-N'-(1,2,3,4-tetrahydro-1-naphthalenyl)-1,4-benzenedimethanamine;
- (jjjj) AMD8768, N,N'-bis(2-pyridinylmethyl)-N'-[(5,6,7,8-tetrahydro-8-quinolinyl)methyl]-1,4-benzenedimethanamine;
- (kkkk) AMD8767, N,N'-bis(2-pyridinylmethyl)-N'[(6,7-dihydro-5H-cyclopenta[bacteriapyridin-7-yl)methyl]-1,4-benzenedimethanamine;
- (llll) AMD8838, N-(2-pyridinylmethyl)-N-(2-methoxyethyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
- (mmmm) AMD8871, N-(2-pyridinylmethyl)-N-[2-(4-methoxyphenyl)ethyl]-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
- (nnnn) AMD8844, N,N'-bis(2-pyridinylmethyl)-1,4-(5,6,7,8-tetrahydro-8-quinolinyl)benzenedimethanamine;
- (oooo) AMD7129, N-[(2,3-dimethoxyphenyl)methyl]-N'-(2-pyridinylmethyl)-N-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
- (pppp) AMD7130, N,N'-bis(2-pyridinylmethyl)-N-[1-(N''-phenyl-N''-methylureido)-4-piperidinyl]-1,3-benzenedimethanamine;
- (qqqq) AMD7131, N,N'-bis(2-pyridinylmethyl)-N-[N''-p-toluenesulfonylphenylalanyl]-4-piperidinyl]-1,3-benzenedimethanamine;
- (rrrr) AMD7136, N,N'-bis(2-pyridinylmethyl)-N-[1-[3-(2-chlorophenyl)-5-methylisoxazol-4-oyl]-4-piperidinyl]-1,3-benzenedimethanamine;
- (ssss) AMD7138, N-[(2-hydroxyphenyl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl]-1,4-benzenedimethanamine;
- (tttt) AMD7140, N-[(4-cyanophenyl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl]-1,4-benzenedimethanamine;
- (uuuu) AMD7141, N-[(4-cyanophenyl)methyl]-N'-(2-pyridinylmethyl)-N-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
- (vvvv) AMD7142, N-[(4-acetamidophenyl)methyl]-N'-(2-pyridinylmethyl)-N-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
- (wwww) AMD7145, N-[(4-phenoxyphenyl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl]-1,4-benzenedimethanamine;
- (xxxx) AMD7147, N-[(1-methyl-2-carboxamido)ethyl]-N,N'-bis(2-pyridinylmethyl)-1,3-benzenedimethanamine;

(yyyy) AMD7151, N-[(4-benzyloxyphenyl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl]-1,4-benzenedimethanamine; and

(zzzz) AMD7155, N-[(thiophene-2-yl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl]-1,4-benzenedimethanamine.

119. (Amended) [The] A compound of [claim 1, wherein W is a nitrogen atom] the  
formula



wherein, W is a nitrogen atom and Y is void;

R<sup>1</sup> to R<sup>7</sup> may be the same or different and are independently hydrogen or straight,

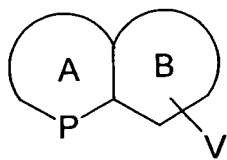
branched or cyclic C<sub>1-6</sub> alkyl;

R<sup>8</sup> is an optionally substituted heterocyclic group or an optionally substituted aromatic  
group

Ar is an aromatic or heteroaromatic ring optionally substituted at single or multiple, non-  
linking positions with electron-donating or withdrawing groups;

n and n' are independently, 0-2;

X is a group of the formula:



wherein, Ring A is an optionally substituted, saturated or unsaturated 5 or 6-membered  
ring, and P is an optionally substituted nitrogen atom and wherein any heteroatom in ring A or B  
is N;

wherein Ring B is an optionally substituted 5 to 7-membered ring;

wherein Ring A or Ring B is bound to group W from any position through group V;

wherein V is a chemical bond or V is a (CH<sub>2</sub>)<sub>n''</sub> group (where n'' = 1-2), or V is a C=O  
group; and



wherein Z is selected from the group consisting of: a hydrogen atom; an optionally substituted C<sub>1-6</sub> alkyl group; an optionally substituted aromatic or heterocyclic group; a C<sub>1-6</sub> alkyl group substituted with an optionally substituted aromatic or heterocyclic group; an optionally substituted amino group; an optionally substituted C<sub>1-6</sub> alkylamino or C<sub>3-7</sub> cycloalkylamino group; a sulfonyl group and an optionally substituted carbonyl group; or the pharmaceutically acceptable acid addition salts thereof;

including said compound in any stereoisomeric form and mixture of stereoisomeric forms thereof.

125. (Amended) The compound of claim 119 wherein said optional substituent in Ring A or Ring B is independently an optionally substituted aralkyl or heterocycloalkyl, wherein said heterocycloalkyl [comprises] is a 5 or 6 membered ring [comprising] containing 1-4 heteroatoms.

129. (Amended) The compound of claim 128, wherein said optionally substituted aromatic group is substituted with a substituent selected from the group consisting of: benzene; naphthalene; dihydronaphthalene; and tetrahydronaphthalene; and wherein said optionally substituted heterocyclic group is [selected from the group consisting of:] a 5 to 6-membered saturated, partially saturated, or aromatic heterocyclic ring [comprising] containing 1 to 4 heteroatoms selected from nitrogen, oxygen and sulfur.

131. (Amended) The compound of claim 130, wherein said heterocyclic group [comprises] contains nitrogen or sulfur heteroatoms; and wherein said nitrogen or sulfur heteroatoms [may] are optionally [be] in the form of oxides.